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Association Between Performance on Timed Up and Go Subtasks and Mild Cognitive Impairment: Further Insights into the Links Between Cognitive and Motor Function

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Abstract

Background—Time to complete the Timed Up and Go (TUG), a test of mobility and fall risk, was recently associated with cognitive function.

Objectives—To assess whether different TUG subtasks are preferentially affected among older adults with mild cognitive impairment (MCI) and are specific to different cognitive abilities.

Design—Cross sectional study

Setting—Community and home setting

Participants—347 older adults without dementia (mean 83.6±3.5yrs, 75% females, 19.3% MCI) participating in the Rush Memory and Aging Project.

Measurements—Subjects wore a small, light-weight sensor that measured acceleration and angular velocity while they performed the instrumented TUG (iTUG). Measures of iTUG were derived from 4 subtasks: walking, turning, sit-to-stand and stand-to-sit and compared between participants with no cognitive impairment (NCI) versus MCI.

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Conflict of interest:

None of the authors report any conflicts of interest.

Results—NCI and MCI did not differ in age, sex, years of education ($p>0.44$) or time to complete the TUG (NCI:7.6±3.7sec vs. MCI:8.4±3.7sec; $p=0.12$). MCI had less walking consistency ($p=0.0091$), smaller pitch range during transitions ($p=0.005$), lower angular velocity during turning, and required more time to complete the turn-to-walk ($p=0.042$). Gait consistency was correlated with perceptual speed ($p=0.012$) and turning was correlated with perceptual speed ($p=0.024$) and visual-spatial abilities ($p=0.049$).

Conclusions—MCI is associated with impaired performance on iTUG subtasks that cannot be identified when simply measuring overall duration of performance. Distinctive iTUG tasks were related to particular cognitive domains, demonstrating the specificity of motor-cognitive interactions. Using a single body worn sensor for quantify of mobility may facilitate our understanding of late-life gait impairments and their inter-relationship with cognitive decline.

Keywords

aging; mild cognitive impairment; accelerometers; gait; cognition

INTRODUCTION

Gait disorders are common among subjects with cognitive impairments^{1,2}. Alterations in walking may be detected early in the course of dementia and even in the prodromal stage of mild cognitive impairment (MCI)³. Motor slowing may precede and predict the onset of cognitive impairment^{4,5}. Furthermore, participants with cognitive decline and slow gait speed (<1.00 m/s) are twice as likely to develop dementia, specifically vascular dementia, compared to subjects with intact cognition and normal gait speeds⁶. Interestingly, the combined motor and cognitive assessment provided better predictive value for dementia than cognitive function alone. These findings highlight the importance of gait assessment for augmenting the early identification and natural progression of neurodegenerative disorders associated with dementia⁶ and support the idea that late-life gait impairments may accompany cognitive decline. Understanding the underpinnings of motor-cognitive changes in MCI is likely to provide important insights into the underlying biology and to provide unique opportunities for interventions that may slow the neurodegenerative process.

The ‘Timed Up and Go’ test (TUG)⁷ is a quick and widely used performance-based measure of mobility. The TUG has been extensively studied in older adults^{8,9} and recommended as a simple screening test of fall risk¹⁰. TUG duration has also been associated with cognitive function^{11,12}. More specifically, older adults with better executive function and attention performed the TUG more quickly^{11,12}. The TUG is composed of several different subtasks including transitions, straight-line walking and turning. Successful completion of the transition and turning sub-tasks of the TUG requires the integration of more cognitive resources than straight-line walking¹¹, perhaps due to the processing of different visual and afferent inputs during straight-line walking and curved walking or turns¹³. If so, different TUG components might be particularly sensitive as predictors of future cognitive decline, more so than just the overall time to complete the TUG. However, the factors that contribute to the association between cognitive function and TUG performance are not well-known.

Previous work has demonstrated the added value of using body-worn sensors to augment the traditional TUG. This approach has been referred to as the instrumented TUG (iTUG)¹⁴. The iTUG allows for the quantitative characterization of the specific components of the TUG and their contribution to overall performance^{15;16}. It is also sensitive to changes in performance, disease progression, and disability^{17;18} and may increase the predictive value for cognitive decline¹⁹. Thus, given the associations between the TUG and cognitive function^{11;12}, we tested the hypothesis that different TUG subtasks might be preferentially affected in MCI. In addition, we tested whether specific TUG subtasks were differentially associated with cognitive abilities.

METHODS

Subjects

Subjects participating in the Rush Memory and Aging Project (MAP), a longitudinal cohort study of chronic conditions of aging²⁰, were studied. Participants were recruited from retirement facilities and subsidized housing facilities from around the Chicago metropolitan area. All participants signed an informed consent agreeing to annual clinical evaluation. The study was approved by the institutional review board of Rush University Medical Center. The hybrid body-worn sensor (see below) was added to the study in 2011 enabling yearly assessment of motor performance. Persons were eligible for this cross-sectional analyses if they were ambulatory, and without clinical dementia (see online methods) at the time of iTUG testing.

Cognitive and Clinical Testing

Subjects underwent a uniform structured clinical evaluation including assessment of medical history, neurological examination, motor and cognitive performance testing. Details of the clinical evaluation are described elsewhere²⁰ and in the online supplementary material.

Timed Up and Go test

To complete the TUG, participants were instructed to stand up from a chair without using arm rests if they were present, walk 8 feet to a designated location at their normal pace, turn around, walk back and sit back down on the same chair⁷. The use of walkers and canes was allowed. Participants wore a portable small, light-weight body-fixed sensor (Hybrid, Microberts, The Hague) on their lower back secured with a neoprene belt. The sensor included tri-axial accelerometer and gyroscope. Acceleration signals were derived from three axes: vertical (V), medio-lateral (ML) and anterior posterior (AP). Angular velocities were derived from the gyroscope as: yaw- the rotation around the vertical axis, pitch- the rotation around the medial-lateral axis, and roll- the rotation around the anterior-posterior axis. The device was set to record continuously during two trials of TUG; data presented are from the 2nd trial. After testing was completed, data were transferred to a personal computer for further analysis using Matlab software (version R2012b).

Quantifying the TUG Subtasks

An automated algorithm based on the anterior-posterior axis was used for detecting the start and end times of the TUG as previously described^{17;21}. In addition, quantitative measures

for 4 subtasks (sit-to-stand and stand-to-sit transitions, walking and turning) were derived (see the online supplementary material).

Statistical Analyses

All data was assessed for normalcy using Komogorov-Smirnov and Shapiro-Wilk tests, and with Levene's test for homogeneity. Student t-tests and the equivalent Mann Whitney compared iTUG measures between the participants with and without MCI. Univariate regression models examined the associations between iTUG measures and the global cognitive score. For each TUG subtask, the corresponding iTUG measure that significantly distinguished between the groups was used as the dependent variable in the models to evaluate motor-cognitive associations (see Table 2 and Table 3). Cognitive measures significantly associated with iTUG measures in univariate models were entered into the multivariate models adjusted for age, sex and education. All analyses were corrected for multiple comparisons using the Benjamini- Hochberg method²². Group values are reported as mean±standard deviation. Statistical analyses was performed using SPSS version 19.

RESULTS

The clinical characteristics of the participants (n=347, 19.3% MCI) are summarized in Table 1. Individuals with no cognitive impairment (NCI) and MCI did not differ with respect to age, sex, years of education or co-morbidities (p>0.44).

TUG Subtask Measures in MCI and NCI

Time to complete the TUG was not significantly different in the two groups (MCI: 8.4±3.7sec vs. NCI:7.6±3.7sec; p=0.12), but iTUG measures differed between MCI and NCI (Table 2).

Walking—Subjects with MCI had lower step regularity (i.e., less consistency of gait) in both the vertical and anterior-posterior directions (Table 2).

Transitions—MCI subjects had lower pitch range and jerk during the transitions from sitting to standing suggesting less forward progression during the movement (Table 2).

Turns—Duration of the turn-to-walk was longer in subjects with MCI and the yaw amplitude was lower in both turns, reflecting lower angular velocity during the turns in the subjects with MCI (Table 2).

TUG Subtask Measures and Cognitive Abilities

The global cognitive score was correlated with gait regularity, pitch range during transitions, and yaw amplitude during turns. In univariate analyses, episodic, semantic, working memory and perceptual speed were correlated with step regularity. Working memory and perceptual speed were correlated with the pitch range during the sit-to-stand transition. Episodic memory, working memory, perceptual speed and visual-spatial ability were correlated with yaw amplitude during the turns (see Table 3). In a multivariate analysis model, perceptual speed remained significantly associated with step regularity during

walking and perceptual speed and visual-spatial abilities were correlated with turning (see Table 3).

DISCUSSION

This study demonstrates that utilizing acceleration and angular velocity signals to quantify the TUG and its subtasks can provide insights into gait performance and its association with cognitive function in older adults. The traditional time to complete the TUG was not significantly different between individuals with and without MCI, however, the groups differed in their performance on the subtasks. Application of the sensors enabled acquiring information about performance that is not merely related to the duration of movement but also to the quality of movement generation. Specifically, measures derived from the sensor revealed higher step irregularity in walking in subjects with MCI, less forward trunk movement during transitions, and less axial rotation during turns. The iTUG appears to differentiate gait performance in older adults with MCI from those with normal cognitive function. Moreover, the results suggest that TUG subtasks may be differentially associated with distinct cognitive abilities.

Several intriguing studies demonstrated that motor slowing may predict the onset of cognitive impairment^{4,5}. Thus, one might expect that gait speed would be slower and hence time to complete the TUG would be longer in MCI subjects. In our study, time to complete the TUG was similar in the NCI and MCI groups. Although surprising, this finding is consistent with other studies^{19,23} which similarly, did not find differences in TUG duration in older adults with and without cognitive decline. A possible explanation could be related to the relatively short duration of walk in the iTUG, which perhaps led to a floor effect or to the increased inter-subject variability in MCI as a result of cognitive reserve²⁴. Nonetheless, specific iTUG components were altered in the subjects with MCI.

Despite its apparent simplicity, the TUG can be viewed as a sequence of complex multiple tasks²⁵. It relies on several distinct aspects of strength, balance, and mobility and coordination of serial movements. Sit-to-stand requires forward movement of the center-of-mass while still seated (in preparation for standing), acceleration in the anterior-posterior and vertical plane, push-off, and finally stabilization once standing is achieved²⁵. The TUG then requires appropriate initiation of stepping, and preparation for turning. Thus, the added value of using the iTUG is the ability to associate the specificity of the task to changes in axial measures and performance. For example, to efficiently transfer from sitting to standing, it is necessary to generate a large pitch, forward elevation moment, initiation of movement and planning. Stand-to-sit, on the other hand, is a quicker, more ballistic movement that requires deceleration of movement but less control. Therefore these measures are highly sensitive to change in performance and as observed, were able to differentiate between the groups. The ability to assess different complex tasks perhaps makes the iTUG more useful clinically and when evaluating early changes in function, than assessing more simple tasks such as straight line walking.

The differences observed in the iTUG subtasks in subjects with MCI may reflect mild motor impairment. These changes are not yet clinically significant, but could represent a decline of

motor function that may parallel mild cognitive impairments. This finding is in line with an earlier study that showed motor decline in individuals with MCI²⁶. Intriguingly, the detection of these alterations, even while gait speed did not differ from that of the cognitively intact controls, suggests that perhaps these measures may be more sensitive than just time to completion or gait speed. Green et al. used gait measures obtained during the iTUG to predict cognitive decline in older adults without dementia in a longitudinal study. At baseline, all participants were cognitively intact and gait speed was similar between groups. After 2 years, 12% demonstrated cognitive decline, however, their gait speed was still intact but quantitative gait measures from the iTUG turn differed between the groups¹⁹. Our study adds to this report by demonstrating that changes can be observed in the different subtasks and that each of the subtasks is unique in identifying early motor changes associated with specific cognitive decline. Although a wide range of gait tests or metrics that capture additional aspects of balance and mobility may be useful for evaluating “motor” function in individuals with MCI, the iTUG is simple and quick to perform, while also capturing multiple domains of motor function, mobility and cognitive function. Hence, it may represent a simple way of augmenting the clinical assessment, with minimal additional costs or time.

Consistent with earlier reports^{11;12}, we found associations between the iTUG and several cognitive domains. Perceptual speed, reflecting executive function abilities, was associated with walking performance on the iTUG. Prolonged time to plan a movement is particularly relevant for TUG, where fluid transitions between consecutive phases of the task are required. The contribution of visual spatial processing to performance of the turn-to-walk transition (both duration and amplitude) is intriguing. Turning-related neural systems may be more vulnerable to functional impairments than straight line gait. Turning involves more inter-limb coordination, more coupling between posture and gait, modification of locomotor patterns requiring frontal lobe cognitive and executive function as well as perception which plays a role in postural transitions. Turning also places greater demands on visual processing to enable clear directional movement¹². A recent factor analysis model of gait posits that domains of pace (speed) and gait variability are related to attention and processing²⁷. The present results support this idea in that slower processing speed was related to TUG performance. Our findings also provide support for the processing speed theory which posits that decline in processing speed reflects a general constraint on all cognitive processing²⁸. This also further reinforces the notion that motor function is associated with cognitive function due to the planning and decision making that is necessary for the successful completion of all movements³.

The mild, but detectable changes in motor function even in a simple test like the iTUG might indicate the beginning of a process that is heading towards more severe disability. These findings may be clinically relevant in older adults because they may provide insight into functional decline in an early stage, when neural substrates still exist and potential preventive interventions can be provided. The iTUG can be used to further enhance the prediction of cognitive impairment⁶, above and beyond gait speed and, therefore, might be useful for assessing patients with early neurodegenerative diseases (e.g., Parkinson's or Alzheimer's disease) as a measure of disease progression that could also inform on increased risk of falls⁶. The results also support recommendations for early intervention to preserve

mobility that should focus on improving specific physical performance of transitions and turns and cognitive function. As the availability of these assessment methods becomes more commonplace in the clinical and research communities, it will have the potential to transform diagnostic and rehabilitation paradigms by providing clinicians with a larger lexicon for describing gait impairment in older adults. It is, however, important to keep in mind that the association between motor and cognitive function in individuals with MCI as found in this cross sectional study may just be the result of a shared common biology due to some underlying latent variables, i.e., not causal³. While this question cannot be resolved in the present study, the associations between specific cognitive features and specific TUG components is consistent with the possibility that TUG performance actually relies on cognitive function.

There are several limitations to our study. The groups were unbalanced in terms of the size of the cohorts (NCI vs. MCI). Since the study was conducted in the participant's homes, we used a slightly shorter distance to assess the TUG and could not fully control the conditions in the home. Nonetheless, we suggest that a difference in length would not change the underlying CNS mechanisms for the planning, initiation and execution of movement. Regardless, the present findings indicate that the iTUG may be a useful tool for detecting early mobility changes in MCI and may also provide clinicians with a sensitive means for assessing functional ability.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Subject characteristics

	MCI	NCI	P-Value
Demographics			
Number of subjects	67	280	
Age (yrs)	83.35±3.50	82.75±4.17	0.901
Sex (% female)	75%	74%	0.804
Body-mass index (kg/m ²)	27.92±5.36	27.22±5.61	0.484
Education (yrs)	15.18±3.35	15.03±2.83	0.447
Vascular Disease Comorbidities score	0.35±0.57	0.34±0.59	0.888
Vascular Risk score	1.24±0.79	1.22±0.83	0.802
Cognitive Function[*]			
Global cognition score	-0.24±0.55	0.33±0.41	P<0.001
Episodic memory score	-0.35±0.81	0.51±0.50	P<0.001
Semantic memory score	-0.15±0.76	0.32±0.59	P<0.001
Working memory score	-0.16±0.73	0.14±0.67	0.002
Perceptual speed score	-0.19±0.68	0.20±0.68	P<0.001
Visual-spatial score	-0.28±0.89	0.28±0.67	P<0.001
Gait			
Gait speed (m/sec)	0.57±0.16	0.48±0.16	0.637

Vascular disease comorbidity score- This variable measures the participants' vascular disease burden computed on the basis of self-report questions, clinical examination, and medication inspection. Vascular Risk score- includes the summary scores indicating each individual's vascular risk burden, computed on the basis of self-report questions, clinical examination, and medication inspection (i.e., sum of hypertension, and smoking).

* Cognitive function is reported using z scores. Higher values reflect better performance.

Table 2

iTUG measures in MCI and NCI

Measure	Axis	MCI	NCI	P-value
Overall TUG				
TUG Duration [s]		8.43±3.72	7.61±3.78	0.121
Walking				
Walking Duration [s]	V	4.98±1.84	4.5±2.06	0.386
Number of steps [#]	V	13.49±5.48	12.13±5.00	0.058
Average step duration [s]	V	0.61±0.64	0.61±0.70	0.724
Step regularity [g ²]	V	0.45±0.13	0.50±0.13	0.009
	AP	0.39±0.15	0.46±0.14	0.002
Step symmetry	V	1.35±0.43	1.36±0.54	0.934
	AP	1.17±0.50	1.33±0.83	0.144
Sit-to-Stand Transition				
Duration [s]	AP	1.04±0.74	0.96±0.80	0.465
Range [g]	AP	0.89±0.27	1.02±0.44	0.036
Jerk [g/s]	AP	-1.08±0.76	-1.67±0.48	0.330
Range [deg/s]	Pitch	151.07±48.43	165.56±54.38	0.005
Jerk [deg/s ²]	Pitch	171.23±103.82	197.12±97.81	0.006
Stand-to-Sit Transition				
Duration [s]	AP	1.01±0.48	0.98±0.51	0.680
Range [g]	AP	1.11±0.38	1.11±0.35	0.863
Jerk [g/s]	AP	1.08±0.63	1.18±0.87	0.349
Range [deg/s]	Pitch	159.65±50.37	161.87±55.38	0.770
Jerk [deg/s ²]	Pitch	132.18±89.12	149.74±98.62	0.194
Turn-to-walk				
Duration [s]	Yaw	2.41±0.67	2.23±0.61	0.042
Yaw Amplitude [deg/s]	Yaw	135.56±41.145	146.32±37.78	0.045
Turn-to-sit				
Duration [s]	Yaw	2.19±0.54	2.17±0.64	0.889
Yaw Amplitude [deg/s]	Yaw	134.36±37.99	144.64±41.10	0.050

Acceleration units are represented by g (gravitational), as they represent force per unit mass Angular velocity collected by the gyroscope is represented in deg/sec.

* P-values that are bolded were statistically significant after adjusting for multiple comparisons.

Table 3

Associations between TUG Subtask Measures and Cognitive Abilities (n=347)

	Univariate model	Multivariate model
Walking (dependent variable: Step regularity [g ²] in the V axis)		
Episodic memory score	0.03 (0.012-0.046) p=0.001	0.02 (-0.003-0.041) p=0.08
Semantic memory score	0.02 (0.002-0.04) p=0.033	-0.02 (-0.047-0.006) p=0.14
Working memory score	0.03 (0.009-0.05) p=0.004	0.009 (-0.013-0.031) p=0.41
Perceptual speed score	0.04 (0.02-0.056) p=0.000	0.04 (0.011-0.059) p=0.004
Visual-spatial score	0.02 (-0.003-0.034) p=0.108	
Sit-to-Stand (dependent variable: Pitch range [deg/s] of transition)		
Episodic memory score	-0.19 (-0.078-0.40) p=0.533	
Semantic memory score	-0.04 (-0.11-0.02) p=0.203	
Working memory score	-0.09 (-0.16—0.26) p=0.007	-0.06 (-0.13-0.012) p=0.102
Perceptual speed score	-0.07(-0.13—0.008) p=0.027	-0.04 (-0.11-0.026) p=0.215
Visual-spatial score	-0.06 (-0.12-0.005) p=0.07	
Turning (dependent variable: yaw amplitude [deg/s] during the turn-to-walk transition)		
Episodic memory score	4.91 (0.41-9.41) p=0.033	-1.23 (-6.55-4.09) p=0.65
Semantic memory score	4.45 (-0.66-9.56) p=0.088	
Working memory score	6.89 (1.81-11.97) p=0.008	0.40 (-5.53-6.34) p=0.89
Perceptual speed score	9.83 (5.03-14.64) p=0.000	6.09 (0.74-11.44) p=0.03
Visual-spatial ability score	8.77 (3.86-13.68) p=0.000	8.68 (2.61-14.74) p=0.05

* Entries are the B values, 95% confidence intervals and the associated p-value. Multivariate model was adjusted for age, sex and years of education.